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EXAMINER	
DEVI, SARVAMANGALA J N	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/630,223	MICHON ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-51 and 53-55* is/are pending in the application.

4a) Of the above claim(s) *12-41,47-51 and 53-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10, 11 and 42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1205008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 12/05/08 in response to the final rejection mailed 06/05/08.

Status of Claims

2) Claims 1-4, 6 and 11 have been amended via the amendment mailed 12/05/08.

Claims 9 and 52 have been cancelled via the amendment mailed 12/05/08.

Claims 1-8, 10-51 and 53-55 are pending.

Claims 1-8, 10, 11 and 42-46 are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' Information Disclosure Statement filed 12/05/08. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

6) The rejection of claims 9 and 52 made in paragraph 19 of the Office Action mailed 06/05/08 under 35 U.S.C § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claims.

7) The rejection of claim 52 made in paragraph 20 of the Office Action mailed 06/05/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 9 made in paragraph 22(h) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

9) The rejection of claims 9 and 52 made in paragraph 22(j) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

10) The rejection of claim 52 made in paragraph 22(g) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

11) The rejection of claims 9 and 52 made in paragraph 25 of the Office Action mailed 06/05/08 under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, already of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, already of record) (Paoletti *et al.*, 1994) as applied to claims 1 and 6 above, and further in view of Wang *et al.* (*PNAS* 95: 6584-6589, 1998, already of record), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Maintained

12) The rejection of claims 1-8, 10, 11 and 42-46 made in paragraph 19 of the Office Action mailed 06/05/08 under 35 U.S.C § 112, first paragraph, as containing new matter, is maintained for part of the reasons set forth therein.

Applicants point to paragraph 53 of the specification and contend that modified polysaccharides as well as native forms purified from bacteria are encompassed within the scope of the polysaccharides incorporated into a conjugate multivalent molecule. The rejection pertaining to this aspect is hereby withdrawn.

With regard to the second aspect of the rejection related to the limitation: '*directly* followed by separation to *isolate* said ..... different types of *purified* bacterial capsular polysaccharide' [Emphasis added] in the claim, Applicants point to paragraphs [55] and [56] of the original specification and state that this part of the specification describes methods of obtaining bacterial capsular polysaccharides by treatment with enzymes or base, followed by separation processes (e.g., differential precipitation, chromatography, and ultrafiltration) to

remove proteins and nucleic acids and to produce '**purified**' capsular polysaccharides. Applicants also point to Example 1 of the original specification at paragraph [77], which apparently discloses base treatment of GBS bacteria directly followed by 'ultrafiltration to remove proteins and nucleic acids'.

Applicants' arguments have been carefully considered, but are not persuasive. Both the disclosures at paragraphs [55], [56] and [77] as well as Applicants' arguments clearly show that what is supported by the as-filed specification is the limitation 'directly followed by separation to isolate *and purify* said ….. different types of purified bacterial capsular polysaccharide', but not the limitation: '*directly* followed by separation to *isolate* said ….. different types of *purified* bacterial capsular polysaccharide' [Emphasis added]. The rejection stands.

13) The rejection of claim 42 made in paragraph 22(b) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for the reason set forth therein.

14) The rejection of claims 43-46 made in paragraph 22(j) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for the reason set forth therein.

Rejection(s) Withdrawn

15) The rejection of claims 42 and the dependent claims 43-45 made in paragraph 18 of the Office Action mailed 06/05/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn. Applicants point to paragraph 38 of the instant specification for support.

16) The rejection of claim 42 made in paragraph 22(a) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claim 42 made in paragraph 22(c) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

18) The rejection of claims 2-4 made in paragraph 22(d) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

19) The rejection of claim 6 made in paragraph 22(e) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim and claim 1.

20) The rejection of claims 10 and 11 made in paragraph 22(h) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to claim 1.

21) The rejection of claim 11 made in paragraph 22(i) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim and claim.

22) The rejection of claims 2-8, 10, and 11 made in paragraph 22(j) of the Office Action mailed 06/05/08 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

23) The rejection of claims 1, 2, 5, 6, 10, 11, 42 and 44 made in paragraph 24 of the Office Action mailed 06/05/08 under 35 U.S.C § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) in view of Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994), is withdrawn in light of Applicants' amendment to the claims and/or the base claims.

24) The rejection of claims 3 and 4 made in paragraph 26 of the Office Action mailed 06/05/08 under 35 U.S.C. § 103(a) as being unpatentable over 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994) as applied to claims 1 and 6 above, and further in view of Paoletti *et al.* (*J. Infect. Dis.* 180: 892-895, 1999), is withdrawn in light of Applicants' amendment to the base claim.

25) The rejection of claims 7 and 45 made in paragraph 27 of the Office Action mailed 06/05/08 under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of

record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994) as applied to claims 6 and 44 above, and further in view of Wessels *et al.* (*J. Infect. Dis.* 171: 879-884, 1995), is withdrawn in light of Applicants' amendment to the base claim.

26) The rejection of claims 8 and 46 made in paragraph 28 of the Office Action mailed 06/05/08 under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994), Wessels *et al.* (*J. Infect. Dis.* 171: 879-884, 1995, of record) as applied to claims 7 and 45 above, and further in view of Michon *et al.* (*In*: *Streptococci and the Host.* (Ed) Horaud *et al.* Plenum Press, New York, pages 847-850, 1997, of record) (Michon *et al.*, 1997) and Laude-Sharp *et al.* (*In*: *Abstracts of the 97th General Meeting of the American Society for Microbiology*, Miami Beach, FL, page 251, # E-62, 1997, of record), is withdrawn in light of Applicants' amendment to the base claim.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

27) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

28) Claims 1-8, 10, 11 and 42-46 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 3, which depends from the amended claim 1, is indefinite, incorrect, and internally inconsistent in the limitations: 'purified bacterial capsular polysaccharide' (see line 2) and 'purified bacterial capsular polysaccharides' (see line 3).

(b) Claim 44 lacks proper antecedent basis in the limitation: 'purified bacterial capsular polysaccharides' (see line 2). Claim 44 depends from claim 42, which already includes the limitation, it is suggested that Applicants provide proper antecedent basis by replacing the limitation with --the purified bacterial capsular polysaccharides--.

(c) Claim 1, as amended, lacks proper antecedent basis in the limitation: 'purified bacterial capsular polysaccharides' (see lines 8 and 9). Since lines 2 and 3 of the claim already

include the limitation, it is suggested that Applicants provide proper antecedent basis by replacing the limitation with --the purified bacterial capsular polysaccharides--.

(d) Claim 42, as amended, lacks proper antecedent basis in the limitation: 'purified bacterial capsular polysaccharides' (see lines 10 and 11). Since lines 4 and 5 of the claim already include the limitation, it is suggested that Applicants provide proper antecedent basis by replacing the limitation with --the purified bacterial capsular polysaccharides--.

(e) Claim 42, as amended, lacks proper antecedent basis in the limitation: 'at least three different types of bacterial capsular polysaccharides' (see last two lines). Since lines 4 and 5 of the claim already include the limitation, it is suggested that Applicants provide proper antecedent basis by replacing the limitation with --at least three different types of the bacterial capsular polysaccharides--.

(f) Claims 2-8, 10 and 11, which depend from claim 1, and claims 43-46, which depend from claim 42, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 103

29) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

30) Claims 1, 2, 5, 6, 10, 11 and 42-44 are rejected under 35 U.S.C § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) in view of Wessels *et al.* (*PNAS* 84:

9170-9174, 1987) (Wessels *et al.*, 1987), Wang *et al.* (*PNAS* 95: 6584-6589, 1998, of record) and Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994).

It is noted that the 'protective antibodies' recited in the independent claims do not exclude anti-carrier protein protective antibodies.

Chong *et al.* disclosed a multivalent immunogenic conjugate molecule comprising a carrier protein such as tetanus toxoid and multiple different purified carbohydrate fragments each linked to the carrier protein and a vaccine comprising the same in a physiologically acceptable carrier. See claims 12, 11, 2 and 1; and paragraphs [0091] to [0095]. Chong *et al.* taught a novel glycoconjugate technology that can be used to covalently link multiple oligosaccharides from Group B *Streptococcus* 'to the same carrier protein' and the multivalent conjugate molecules produced thereby. See section [0057]. The conjugate components are present in equimolar amounts and induce anti-carrier antibodies. See section [0084]. Chong's multivalent immunogenic conjugate molecule is expected to elicit anti-tetanus toxoid antibodies that are known in the art to be protective.

Chong *et al.* do not expressly identify multiple oligosaccharides of Group B *Streptococcus* to be at least three types such as types Ia, Ib, II and III GBS capsular oligosaccharides of molecular weight in the range of 80-120 kDa.

However, the depolymerised GBS capsular polysaccharides of desired size, including those that fall in the range between 80 and 120 kilodaltons, or less than 100 kilodaltons, and a method of preparing them were known in the art at the time of the invention. For example, Wessels *et al.* (1987) taught oligosaccharides of a GBS capsular polysaccharide having a molecular weight of 98,000 and their increased reactivity with or increased affinity for GBS type III antiserum. See Table 1' abstract; and first paragraph under 'Materials and Methods'.

Methods of preparing depolymerised GBS capsular polysaccharides of desired size were known in the art at the time of the invention. For instance, Wang *et al.* taught the process of selectively depolymerizing GBS types I-VIII capsular polysaccharides to desired size by controlled treatment of the full-length capsular polysaccharides with ozone, without affecting the labile sialic acid residues of the polysaccharides. See abstract; 'Materials and Methods'; section 'Kinetics' on page 6587; first paragraph under 'Results and Discussion'; and page 6588 including the first full paragraph in right column.

Paoletti *et al.* (1994) taught different purified types Ia, Ib, II and III of Group B *Streptococcus* capsular polysaccharides, purified according to reference 32 cited therein, and the concept of having, in a multivalent conjugate vaccine, said at least four different purified Group B *Streptococcus* capsular polysaccharides, to elicit protective antibodies against the capsular polysaccharides, upon covalent linking to tetanus toxoid via 7-29% of the sialic acid residues oxidized. See abstract; Materials and Methods; Tables 1, 2, 5 and 6; Figure 1; and pages 3237 and 3238.

Given that depolymerised GBS capsular polysaccharides having a molecular weight of 98,000 and having increased reactivity with or increased affinity for the corresponding antiserum were already known in the art at the time of the invention as taught by Wessels *et al.* (1987) and given that methods of purifying types Ia, Ib, II and III Group B *Streptococcus* capsular polysaccharides and methods of preparing depolymerised GBS capsular polysaccharides of desired size of capsular polysaccharides of different GBS types without affecting their labile sialic acid residues were known in the art at the time of the invention as taught by Paoletti *et al.* and Wang *et al.* respectively, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to obtain 98,000 molecular weight oligosaccharides of Paoletti's (1994) purified types Ia, Ib, II and III of Group B *Streptococcus* capsular polysaccharides using Wang's method of ozone depolymerization and covalently link said oligosaccharides to the same tetanus toxoid carrier protein using Chong's novel glycoconjugate technology to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing one multivalent conjugate comprising capsular oligosaccharides of multiple GBS types wherein sialic acid residues are retained and wherein the conjugate elicits protective antibodies against multiple GBS capsular polysaccharides.

Claims 1, 2, 5, 6, 10, 11 and 42-44 are *prima facie* obvious over the prior art of record.

31) Claims 3 and 4 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) as modified by Wessels *et al.* (*PNAS* 84: 9170-9174, 1987, of record) (Wessels *et al.*, 1987), Wang *et al.* (*PNAS* 95: 6584-6589, 1998, of record) and Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994) as applied to claims 1

and 6 above, and further in view of Paoletti *et al.* (*J. Infect. Dis.* 180: 892-895, 1999, of record) (Paoletti *et al.*, 1999).

The teachings of Chong *et al.* as modified by Wessels *et al.* (1987), Wang *et al.* and Paoletti *et al.* (1994) are explained above which do not teach the number of different types of purified GBS capsular polysaccharides to be five or six.

However, additional purified capsular polysaccharides of GBS type VI and type VIII and the importance of including these types in a conjugate vaccine were known in the art at the time of the invention. For example, Paoletti *et al.* (1999) taught that GBS types VI and VIII are prevalent serotypes isolated from pregnant women in Japan. Paoletti *et al.* (1999) taught purified capsular polysaccharides of GBS types VI and VIII which upon conjugation induced protective antibodies. Paoletti *et al.* (1999) expressly suggested GBS types VI and VIII to be important components of a multivalent GBS vaccine for use in regions where these serotypes are predominate. See abstract; Materials and Methods; and Results.

Given Paoletti's (1999) express teaching that GBS types VI and VIII are prevalent serotypes isolated from pregnant women in Japan, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to obtain 98,000 molecular weight oligosaccharides of Paoletti's (1999) purified type VI and type VIII capsular polysaccharides of Group B *Streptococcus* using Wang's method of ozone depolymerization and covalently link said oligosaccharides to the same tetanus toxoid carrier protein in Chong's novel multivalent glycoconjugate as modified by Wessels *et al.* (1987), Wang *et al.* and Paoletti *et al.* (1994) to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent GBS vaccine that also includes GBS types VI and VIII for use in regions where these serotypes are predominate as taught by Paoletti *et al.* (1999).

Claims 3 and 4 are *prima facie* obvious over the prior art of record.

32) Claims 7 and 45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) as modified by Wessels *et al.* (*PNAS* 84: 9170-9174, 1987) (Wessels *et al.*, 1987), Wang *et al.* (*PNAS* 95: 6584-6589, 1998, of record) and Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994) as applied to claims 6 and

44 above, and further in view of Wessels *et al.* (*J. Infect. Dis.* 171: 879-884, 1995, of record) (Wessels *et al.*, 1995).

The teachings of Chong *et al.* as modified by Wessels *et al.* (1987), Wang *et al.* and Paoletti *et al.* (1994) are explained above, which do not teach type V GBS purified polysaccharide to be a part of their multivalent conjugate molecule.

However, Wessels *et al.* (1995) taught of the recognition in the art of type V strains of GBS as frequent cause of GBS infections in both infants and adults. Wessels *et al.* (1995) taught purified GBS V capsular polysaccharide and showed that it produces protective antibodies on conjugation to a protein. Wessels *et al.* (1995) expressly suggested the inclusion of type V GBS conjugate in a multivalent GBS vaccine for human use. See abstract.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to obtain 98,000 molecular weight oligosaccharides of Wessel's (1995) purified type V GBS capsular polysaccharide using Wang's method of ozone depolymerization and covalently link said oligosaccharides to the same tetanus toxoid carrier protein in Chong's novel multivalent glycoconjugate as modified by Wessels *et al.* (1987), Wang *et al.* and Paoletti *et al.* (1994) to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent GBS vaccine that also includes type V capsular polysaccharide for use in humans in whom type V GBS is a frequent cause of GBS infections as taught by Wessels *et al.* (1995).

Claims 7 and 45 are *prima facie* obvious over the prior art of record.

33) Claims 8 and 46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, of record) as modified by Wessels *et al.* (*PNAS* 84: 9170-9174, 1987) (Wessels *et al.*, 1987), Wang *et al.* (*PNAS* 95: 6584-6589, 1998, of record), Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, of record) (Paoletti *et al.*, 1994), and Wessels *et al.* (*J. Infect. Dis.* 171: 879-884, 1995, of record) (Wessels *et al.*, 1995) as applied to claims 7 and 45 above, and further in view of Michon *et al.* (*In*: *Streptococci and the Host*. (Ed) Horaud *et al.* Plenum Press, New York, pages 847-850, 1997, of record) (Michon *et al.*, 1997) and Laude-Sharp *et al.* (*In*: *Abstracts of the 97th General Meeting of the American Society for Microbiology*, Miami Beach, FL, page 251, # E-62, 1997, of record).

The teachings of Chong *et al.* as modified by Wessels *et al.* (1987), Wang *et al.*, Paoletti *et al.* (1994) and Wessels *et al.* (1995) are explained above which do not teach the carrier protein to be C beta protein.

However, the use of C beta protein as a protein carrier in a multivalent GBS capsular polysaccharide conjugate was known in the art at the time of the invention. For instance, Michon *et al.* (1997) disclosed the use of C protein carrier as an alternative to tetanus toxoid protein carrier in producing a multivalent GBS capsular polysaccharide conjugate. Michon *et al.* (1997) taught that beta C protein is a good carrier protein whose conjugation to different GBS type capsular polysaccharides does not alter its antigenicity. See sections 1 and 4.

Laude-Sharp *et al.* taught the advantages of using streptococcal C-beta protein as a carrier protein in a combination conjugate vaccine against multiple serotypes of Group B *Streptococcus*. Laude-Sharp *et al.* conjugated the streptococcal C-beta protein to the capsular polysaccharides of different types of GBS and showed that besides its carrier function, the C beta protein afforded protection against GBS strains not covered by capsular polysaccharides in the vaccine. In addition to providing protection against different GBS types used, the conjugate vaccine provided additional protection against GBS type Ib. See title and entire disclosure.

Given Michon's (1997) express teaching that beta C protein is a good carrier protein whose conjugation to different GBS type capsular polysaccharides does not alter its antigenicity, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace the tetanus toxoid protein carrier in Chong's multivalent GBS conjugate as modified by Wessels *et al.* (1987), Wang *et al.*, Paoletti *et al.* (1994) and Wessels *et al.* (1995) with Michon's (1997) C beta protein to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of producing a multivalent GBS conjugate vaccine wherein multiple different GBS type capsular polysaccharides are conjugated to streptococcal beta C protein, which multivalent conjugate not only advantageously confers immunity against multiple GBS types, but also affords protection via C-beta protein against GBS strains not covered by the capsular polysaccharides in the vaccine and provides additional protection against GBS type Ib as taught by Laude-Sharp *et al.*

Claims 8 and 46 are *prima facie* obvious over the prior art of record.

Relevant Prior Art

34) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Wang *et al.* (US 6,027,733) taught a method of generating saccharide fragments or depolymerized polysaccharides including capsular polysaccharides of GBS types using ozonolysis. See entire document including claim 30.

Remarks

35) Claims 1-8, 10, 11 and 42-46 stand rejected.

For clarity, in lines 4, 5 and 7 of claim 1; line 3 of claims 2-4; and line 2 of claim 6, it is suggested that Applicants replace the limitation 'purified bacterial capsular polysaccharides' with the limitation --the purified bacterial capsular polysaccharides--.

To be consistent with the language used in line 2 of claim 11, it is suggested that Applicants delete the limitation 'bacterial' from line 2 of claim 10.

36) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

37) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

38) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

39) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

March, 2009